

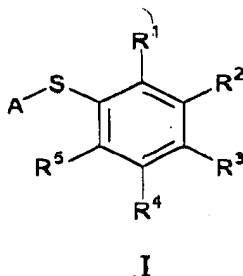
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IN THE CLAIMS:

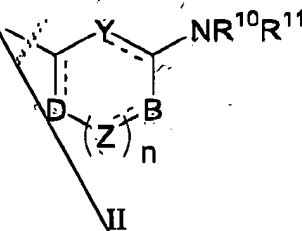
Please amend claims 1-9 and add new claims 10-27 as follows.

1. (Amended) A compound of formula I



or a pharmaceutically acceptable salt or prodrug thereof,

wherein R¹, R², R³, R⁴ and R⁵ are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, carboxaldehyde, and a group of formula II defined as



subject to the proviso that one or more than one of R¹ or R³ is a group of formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR⁶=, -CR⁷R⁸-, C(O)-, -O-, -SO₂-, -S-, -N=, and -NR⁹-;

n is an integer of zero to three;

09/888,840

13780-2/226A/CO93.US CP2

R^6 , R^7 , R^8 , and R^9 , at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R^{13} , wherein R^{13} , at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

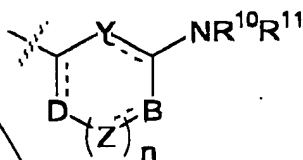
wherein A is an unsubstituted aryl group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than one substituent R^{12} , wherein R^{12} , at each occurrence, is independently selected from the group consisting of halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamido, alkoxycarbonylalkyl, carboxy, carboxyalkyl,

09/888,840

13780-2/226A/CO93.US CP2

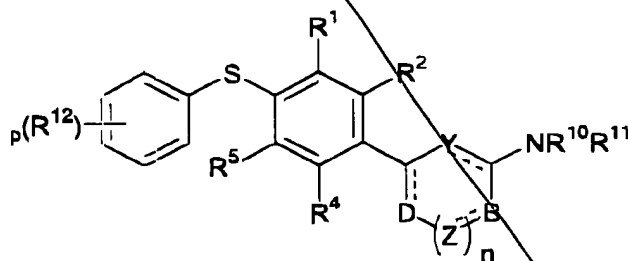
carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclalkylamino, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl and heterocyclalkylaminocarbonyl; and wherein $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}$ and R^{13} are unsubstituted or substituted with one or more than one electron donating or electron withdrawing group.

2. A compound according to claim 1 wherein R^3 is the group of formula II

II

wherein $R^{10}, R^{11}, D, B, Y, Z$, and n are defined as in claim 1.

3. (Amended) A compound according to claim 1 of formula III

III

wherein $R^1, R^2, R^4, R^5, R^{10}, R^{11}, R^{12}, D, B, Y, Z$, and n are defined as in claim 1; and p is an integer of zero to five.

4. (Amended) A compound according to claim 3 wherein p is one;

R^4 and R^5 are hydrogen;

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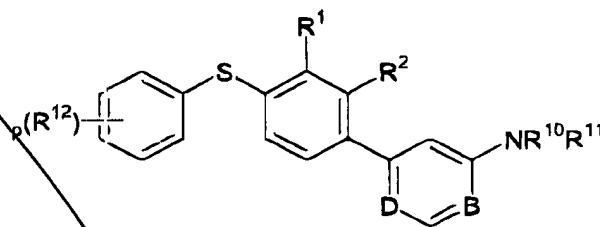
13780-2/226A/CO93.US CP2

R^{12} is selected from the group consisting of halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R^{13} , wherein R^{13} is defined as in claim 1, and wherein said substituted heterocyclyl, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine; and

wherein R^{10} , R^{11} , R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group.

5. (Amended) A compound according to claim 1 of formula IV



IV

wherein D and B are each independently selected from the group consisting of -N= and -CR⁶=;

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are defined as in claim 1;

R^{12} , at each occurrence, is independently selected from the group consisting of halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and

09/888,840

13780-2/226A/CO93.US CP2

heterocyclyl, wherein R^{12} is unsubstituted or substituted with at least one electron donating group or electron withdrawing group; and

p is an integer of zero to five.

6. (Amended) A compound according to claim 5 wherein p is one; and

R^{10} and R^{11} are taken together with N to form a three to seven membered substituted heterocyclyl ring, or a three to seven membered unsubstituted heterocyclyl ring, substituted with one or more substituents R^{13} , wherein R^{13} is defined as in claim 1, and wherein said substituted heterocyclyl ring, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine.

7. (Amended) A compound according to claim 1 selected from the group consisting of 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(3-(2H-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(4-(2H-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-3-yl)-methanol, 2-(1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-yl)-ethanol, N-(1-(4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidin-3-yl)-acetamide, 1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-ol, N-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acetamide, N-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acetamide, N-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acetamide, 4'-(4-(2,3-dihydro-benzo (1,4) dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2H-(1,2') bipyridinyl-4-carboxylic acid, and 4'-(4-(2,3-dihydrobenzo (1,4) dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2H-(1,2')(bipyridinyl-3-carboxylic acid.

09/888,840

13780-2/226A/CO93.US CP2

8. (Amended) A composition comprising:

a compound according to claim 1

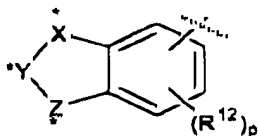
and a pharmaceutically acceptable carrier.

9. (Amended) A method of inhibiting inflammation or suppressing immune response in a mammal comprising administering to said mammal a therapeutic amount of a compound according to claim 1.

10. (New) A compound according to claim 1 wherein A is

(i) an unsubstituted or substituted aryl group, substituted by one or more than one substituent R^{12} , wherein R^{12} is defined as in claim 1, or

(ii) an unsubstituted or substituted heterocyclyl group of the formula



wherein

R^{12} and is defined as in claim 1;

p is an integer of 0 to 5;

X^* and Z^* are each independently selected from the group consisting of $-CH_2-$, $-CH_2NH-$, $-CH_2O-$, $-NH-$, and $-O-$, with the proviso that at least one of X^* and Z^* is not $-CH_2-$; and

Y^* is $-(C(R''))_v-$, wherein

R'' is hydrogen or alkyl; and

v is 1, 2, or 3.

09/888,840

13780-2/226A/CO93.US CP2

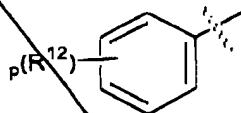
11. (New) A compound according to claim 1 or 10 wherein A is an unsubstituted or substituted aryl group, wherein the aryl group is

- (i) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings or
- (ii) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings wherein one or more than one of the aromatic rings is fused to a ring selected from the group consisting of cyclohexane, cyclohexene, cyclopentane, and cyclopentene.

AS

12. (New) A compound according to claim 1 wherein A is an unsubstituted or substituted aryl group of the formula

Sub
A4



wherein R^{12} is defined as in claim 1; and p is an integer of 0 to 5.

13. (New) A compound according to claim 1 wherein

D is $-CR^6=$ or $-N=$,

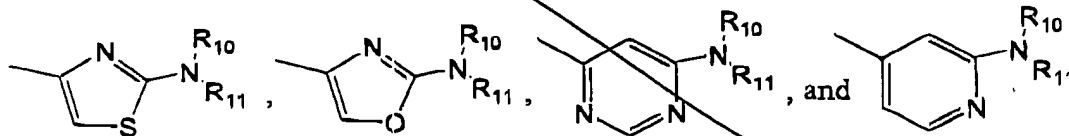
B is $-S-$, $-O-$, $-CR^6=$ or $-N=$,

Y is $-CR^6=$ or $-N=$,

Z is $-CR^6=$ or $-N=$; and

n is zero or one.

14. (New) A compound according to claim 1 wherein R^3 is selected from the group consisting of



09/888,840

13780-2/226A/CO93.US CP2

15. (New) A compound according to claim 1 wherein

D is $-\text{CR}^6=$;B is $-\text{O}-$ or $-\text{S}-$;Y is $-\text{N}=$; and

n is zero.

AS 16. (New) A compound according to claim 1 wherein

D is $-\text{CR}^6=$ or $-\text{N}=$;B is $-\text{N}=$;Y is $\text{CR}^6=$; and

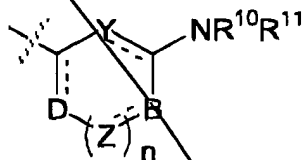
n is 1.

17. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, alkyl, and nitro;

R^4 and R^5 are each independently selected from the group consisting of hydrogen and alkyl; and

R^3 is



wherein

D is $-\text{CR}^6=$ or $-\text{N}=$,

B is $-\text{S}-$, $-\text{O}-$, $-\text{CR}^6=$ or $-\text{N}=$,

09/888,840

13780-2/226A/CO93.US CP2

Y is $-\text{CR}^6=$ or $-\text{N}=\text{}$,

Z is $-\text{CR}^6=$ or $-\text{N}=\text{}$; and

n is zero or one.

Sub
B4
AS
18. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl; and

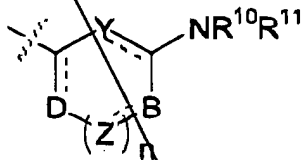
R^4 and R^5 are each independently hydrogen.

19. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is



wherein

D is $-\text{CR}^6=$ or $-\text{N}=\text{}$,

B is $-\text{S}-$, $-\text{O}-$, $-\text{CR}^6=$ or $-\text{N}=\text{}$,

Y is $-\text{CR}^6=$ or $-\text{N}=\text{}$,

Z is $-\text{CR}^6=$ or $-\text{N}=\text{}$; and

n is zero or one.

20. (New) A compound according to claim 1 wherein

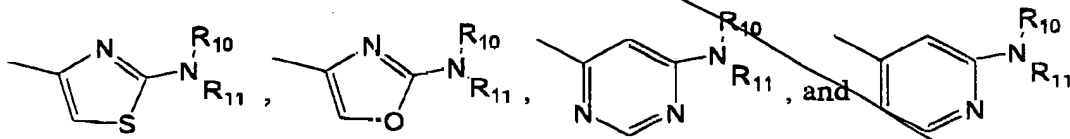
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13780-2/226A/CO93.US CP2

~~R¹ and R² are each independently are selected from the group consisting of hydrogen, chloro, and trifluoromethyl;~~

~~R⁴ and R⁵ are each independently hydrogen; and~~

~~R³ is selected from the group consisting of~~



21. (New) A compound according to claim 1 wherein R⁶ is hydrogen.

22. (New) A compound according to claim 1 wherein

R¹ is selected from the group consisting of hydrogen, halogen and haloalkyl,

R² is selected from the group consisting of hydrogen and halogen, and

R⁴ and R⁵ are each independently hydrogen.

23. (New) A compound according to claim 22 wherein

R¹ is trifluoromethyl, and

R² is hydrogen.

24. (New) A compound according to claim 22 wherein R¹ and R² are each independently chloro.

25. (New) A compound according to claim 1 which has an IC₅₀ of less than 20 μM when tested in one or both of

(i) an ICAM-1/LFA-1 Biochemical Interaction Assay, or

(ii) an ICAM-1/JY-8 Cell Adhesion Assay.

09/888,840

13780-2/226A/CO93.US CP2

AS 26. (New) A method for ameliorating a pathology in a mammal arising from the interaction of LFA-1 with ICAM-1 or ICAM-3 comprising administering to said mammal a therapeutic amount of a compound according to claim 1.

27. (New) A method according to claim 26 wherein the pathology is selected from an inflammatory disease, an autoimmune disease, tumor metastasis, allograft rejection and reperfusion injury.
